Tetrahedron 70 (2014) 5415–5419

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Facile and efficient synthesis of C_2-symmetrical 1,3,5-triazine polycarboxylate ligands under microwave irradiation

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ARTICLE INFO

Article history:
Received 28 April 2014
Received in revised form 20 June 2014
Accepted 30 June 2014
Available online 3 July 2014

Keywords:
1,3,5-Triazine derivatives
Polycarboxylated ligands
C_2-symmetrical
Metal-organic frameworks
Microwave-assisted synthesis

ABSTRACT

A rapid and efficient method for preparation of C_2-symmetrical 1,3,5-triazine polycarboxylate ligands was developed. The reactions included either selective mono- or di-substitution of 2,4,6-trichloro-1,3,5-triazine with various nucleophiles containing carboxyl group(s), followed by nucleophilic displacement of the remained chloride(s) in aqueous media under microwave irradiation. Novel C_2-symmetrical tripodal ligands were afforded in good yields and purities under short reaction time with simple work-up, which are potentially useful as structural directing units in metal-organic frameworks.

1. Introduction

Metal-organic frameworks (MOFs) or coordination polymers have become increasingly important in many research fields due to their interesting structural novelty and potential applications in catalysis, fluorescent lighting, and chemical sensors.[1–3] Based on the shapes of the organic molecules and the specific interactions within the frameworks, formation of complex structural architectures with intriguing properties can be achieved.

Flexible ligands containing three or more carboxyl groups are highly desirable since they can induce a number of coordination modes allowing formation of interesting structures with higher dimensionalities.[4] In addition, each carboxyl groups can form different dihedral angles, which may coordinate to metal in various orientations.

So far, a number of flexible C_3-symmetrical polycarboxylic ligands based on 1,3,5-triazine core have been introduced as the structural directing units in the construction of novel functional MOFs.[4–11] These ligands such as *N*,*N*′,*N*″-1,3,5-triazine-2,4,6-triyltris-glycine (TTG),[12–14] 1,3,5-triazine-2,4,6-triamine hexaacetic acid (TTHA),[14] 1,3,5-triazine-2,4,6-piperidine-4-carboxylic acid,[15] 1,3,5-triazine-2,4,6-trithiotri-3-benzoic acid,[10] and 1,3,5-triazine-2,4,6-triaminetri-4-benzoic acid[16,17] could be easily prepared from a cheap and readily available 2,4,6-trichloro-1,3,5-triazine (TCT). However, due to synthetic difficulty, only one study reported the use of C_2-symmetrical triazine ligands including 1,3,5-triazine-2-iminodiacetic acid-4,6-biglycine, **L1**, and 1,3,5-triazine-2-iminodiacetic acid-4,6-bis(L-alanine), **L2**, in constructing luminescent lanthanide coordination polymers (Fig. 1).[6] It is thus of great interest to develop a rapid and efficient method for synthesis of C_2-symmetrical polycarboxylic triazine-based ligands, which will be potentially useful in MOFs design and synthesis.

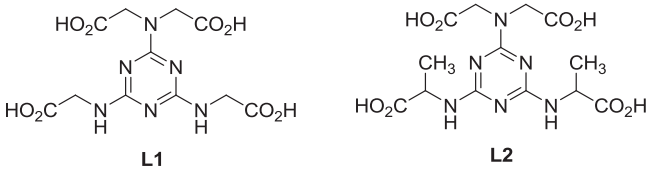

Fig. 1. Examples of C_2-symmetrical 1,3,5-triazine ligands.

Recently, we have reported a microwave-assisted S_NAr reaction for the rapid synthesis of C_3-symmetrical 1,3,5-triazine polycarboxylate ligands using water as the solvent.[18] On continuing this study, we describe the synthesis of C_2-symmetrical carboxylate ligands based on a 1,3,5-triazine core by the selective formation of mono- and di-substitutions triazine derivatives, followed by nucleophilic displacement of the remained chloride(s) with various amino acids under microwave irradiation.

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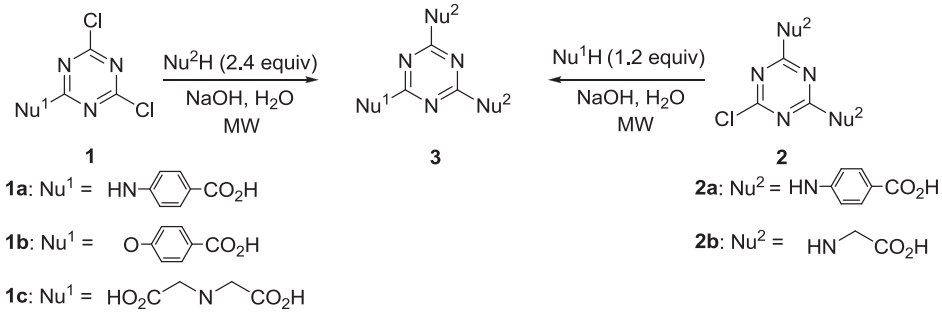
http://dx.doi.org/10.1016/j.tet.2014.06.127
0040-4020/

2. Results and discussion

Due to the difference in the reactivity of the chloride atoms of TCT toward nucleophiles, ideally, C_2-symmetrical carboxylate ligands should be accessible selectively by the stepwise addition of different nucleophiles in one-pot.[19] By the careful control of the reaction temperature, it is commonly observed that mono-substitution of chlorine with amine nucleophiles occurs at ca. 0 °C, di-substitution at room temperature, while tri-substitution proceeds above 60 °C.

Nevertheless, since most trisubstituted triazines containing polycarboxylic acid are not soluble in common organic solvents except in DMSO, the sequential addition of different nucleophiles to TCT with <100% conversion in each step will results in a mixture of trisubstituted products, which are unable to purify by conventional means.

In fact, C_2-symmetrical trisubstituted 1,3,5-triazine core have to be synthesized from mono- or disubstituted TCT derivatives (Scheme 1). Monosubstituted TCT **1a**,[17] **1b**,[20] and **1c**[6] can be prepared selectively by substitution of one chloride atom of TCT with selected nucleophile using 1:1 mol ratio at 0–5 °C according to the reported procedures. Disubstituted TCTs **2a**[17] and **2b**[21] were also similarly obtained by the reaction between TCT and amino acids (1:2 mol ratio) at 0 °C to room temperature.



Scheme 1. Synthesis of C_2-symmetrical 1,3,5-triazine polycarboxylate ligand **3**.

Finally, multidirectional ligands were synthesized under microwave irradiation at 180 W according to our previously reported procedure for preparation of C_3-symmetrical TCT carboxylate ligands. As summarized in Table 1, C_2-symmetrical trisubstituted triazine derivatives **3** can be obtained either by nucleophilic substitution of the two chloride atoms of TCT **1** using 2.4 equiv of nucleophile (entries 1–9) or by displacement of the third chloride atom of TCT **2** with 1.2 equiv of amino acid (entries 10–13) according to Scheme 1.

Due to the difference in nucleophilicity between an amino group and a carboxylate ion, chemoselectivity of the substitutions can be achieved without the requirement of protecting groups. A variety of amino acids containing primary, secondary, or aromatic amine nucleophile were reacted smoothly with the TCT derivatives under short reaction times (within 10–20 min). With a simple aqueous work-up, the corresponding trisubstituted products were afforded in good yields and high purities (>95% based on ^{1}H NMR analysis).

Compared with conventional stirring and heating, using microwave conditions allows various polycarboxylate ligands to be prepared in high yields with very short reaction times. For example, within 10 min microwave irradiation, ligand **3g** and **3h** were obtained in 84% and 75%, respectively (Table 1, entries 7 and 8), whereas under the conventional heating at 105 °C for 12 h, ligand **3g** was obtained in 85% yield, while ligand **3g** was obtained in 65% yield emphasizing the effect of microwave in enhancing the rate of the reaction.[6]

It is worth noting that although it is possible to synthesize trisubstituted ligands **3** from TCT **1** or **2** (see Table 1, entries 7 and 13, 9 and 11), the process is more feasible using **1** as the starting material. The synthesis of monosubstituted TCT **1** is less complicated when compared with that of the disubstituted TCT **2**, while isolation of the trisubstituted product **3** from the remained starting TCT **1** (whenever necessary) is much easier due to the difference in their polarity and solubility. Nevertheless, whenever applicable, final chloride substitution of disubstituted TCT derivatives with weak nucleophiles should be avoided since this displacement step is often problematic requiring harsh conditions and long reaction time. For example, in the stepwise synthesis of 1,3,5-triazine-2,4,6-triaminetri-4-benzoic acid,[17] the third substitution with 4-aminobenzoic acid required 48 h under refluxing in water–acetone mixture. Using our developed procedure, ligand **3i** was rapidly obtained within 20 min either from the mono-substituted TCT **1c** or the disubstituted TCT **2a**, though the yield obtained from **1c** (entry 9, 61%) was slightly lower than those starting from **2a** (entry 11, 75%). In an attempt to displace the two chlorides of **1c** with 4-hydroxybenzoic acid, pure product was unable to isolate due to incomplete conversion even after 30 min microwave irradiation at 180 W. Attempts to drive the reaction to completion by raising the microwave power under prolonged irradiation still failed to give good conversion.

3. Conclusions

In summary, a fast and effective method to prepare C_2-symmetrical 1,3,5-triazine polycarboxylate ligands has been developed. A variety of multipodal ligands with potential applications in the MOFs design were readily obtained in good yields from low-cost commercially available materials in short reaction times using water as the eco-friendly solvent. All products were obtained in high purities from a simple aqueous work-up without requirement of column chromatography. Study on the complexation of these multidirectional ligands with various metals is underway and will be reported in due course.

4. Experimental

4.1. Material and methods

All reagents were purchased from Fluka and Aldrich and were used without further purification. Microwave reactions were conducted using a modified microwave oven (Samsung GB872, 850 W,